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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/789,222
Filing Date	February 24, 2004
First Named Inventor	Qin Yu
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Total Number of Pages in This Submission: 14	Attorney Docket Number: UPN0003-100 (P3115)

ENCLOSURES *(check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment / Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☒ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) ____
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to Group **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) *(please identify below)*:

  References AA-DT

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	David A. Sadewasser/Reg. No. 55,587
Signature	David A. Sadewasser
Date	May 24, 2004

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Typed or printed name	David A. Sadewasser		
Signature	David A. Sadewasser	Date	May 24, 2004

UPN0003-100 (P3115) PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: Qin Yu

Serial No.: ~~10/789~~,222 Group Art Unit: Not Yet Assigned

Filing Date: February 27, 2004 Examiner: Not Yet Assigned

For: ANGIOPOIETIN AND FRAGMENTS MUTANTS AND ANALOGS THEREOF AND USES OF THE SAME

DATE OF DEPOSIT: May 24, 2004
I HEREBY CERTIFY THAT THIS PAPER IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL, POSTAGE PREPAID ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450

David A. Sadewasser
TYPED NAME: David A. Sadewasser
REGISTRATION NO:55,587

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 C.F.R. §§ 1.56 and in accordance with 37 C.F.R. §§ 1.97 and 1.98, information relating to the above-identified application is hereby disclosed, the Examiner in charge of the above-identified application is requested to consider and make of record the references listed on the PTO Form SB/08A and PTO Form SB/08B, formerly known as PTO Form 1449 submitted herewith.

Inclusion of the information submitted herewith is not to be construed as an admission that the information is material as that term is defined in 37 C.F.R. § 1.56(b).

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made.

This Information Disclosure Statement is being filed:

☒ within three months of the filing date of the patent application.

☐ within three months of the date of entry into the national stage as set forth in 37 C.F.R. § 1.491 of the international application.

☐ **before** the mailing date of a first Office Action on the merits.

☐ **after** the mailing date of a first Office Action on the merits, but before the mailing date of a Final Office Action under 37 C.F.R. § 1.116 or a Notice of Allowance under 37 C.F.R. § 1.311, and accordingly is accompanied by:

- ☐ the Statement under 37 C.F.R. § 1.97(e) (see "Statement" below);

or

- ☐ the Fee of $180.00 set forth in 37 C.F.R. § 1.17(p); or
- ☐ No fee is owed by the applicant(s).

☐ In accordance with 37 C.F.R. § 1.129(a), this Information Disclosure Statement is being filed in connection with ☐ the first or ☐ second After Final Submission, and accordingly is accompanied by the Statement under 37 C.F.R. § 1.97(e) (see "Statement" below) and the fee of $180.00 as set forth in 37 C.F.R. § 1.17(p), is attached.

☐ **after** the mailing date of a Final Office Action under 37 C.F.R. § 1.116 or a Notice of Allowance under 37 C.F.R. § 1.311, but before, or simultaneously with, the payment of the Issue Fee, and accordingly is accompanied by the Statement under 37 C.F.R. § 1.97(e), a Petition requesting consideration of the Information Disclosure Statement and the Petition Fee of $130.00 set forth in 37 C.F.R. § 1.17(i)(1) (see "Statement," "Petition," and "Fees" below).

☐ Copies of references (AA-DT) listed on the attached PTO Form SB/08A and PTO Form SB/08B, formerly known as PTO Form 1449 are enclosed.

EXCEPT THAT:

- ☐ In view of the voluminous nature of reference @@, and the likelihood that this reference is available to the Examiner, copies are not enclosed herewith.
- ☐ In accordance with 37 C.F.R. § 1.98(d), copies of the following references listed on the attached PTO Form SB/08A and PTO Form SB/08B, formerly known as PTO Form 1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C. § 120 have been made in the instant application.

☐ Copies of references listed on the attached PTO Form SB/08A and PTO Form SB/08B, formerly known as PTO Form 1449 were previously cited by or submitted to the U.S. Patent and Trademark Office in parent application Serial No. @@.

☐ If any of the foregoing publications are not available to the Examiner, Applicant will endeavor to supply copies at the Examiner's request.

Statement under 37 C.F.R. § 1.97(e)

☐ The undersigned attorney hereby states that each item information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign patent application not more than three months prior to the filing of the Information Disclosure Statement.

Statement under 37 C.F.R. § 1.704(d)

☐ The undersigned attorney hereby states that each item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart application and the communication was not received by any individual designated in §1.56(c) more than 30 days prior to the filing of the Information Disclosure Statement.

Fees

☒ No Fee is owed by the applicant(s).

☐ The Information Disclosure Statement Fee of $180.00 under 37 C.F.R. § 1.17(p) is enclosed herewith.

☐ The Petition Fee of $130.00 under 37 C.F.R. § 1.17(i)(1) is enclosed herewith.

Method of Payment of Fees

☐ Attached is a check in the amount of $_____. This form is submitted in duplicate.

☐ Charge Deposit Account No. 50-1275 in the amount of $_____. This form is submitted in duplicate.

☒ Please charge any deficiency or credit any overpayment to Deposit Account 50-1275.

☒ No fee or Statement is required under 37 C.F.R. § 1.97(b).

Respectfully submitted,

David A. Sadewasser

Dated: May 24, 2004

David A. Sadewasser
Registration No. 55,587

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 9

Complete if Known	
Application Number	10/789,222
Filing Date	February 27, 2004
First Named Inventor	Qin Yu
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	UPN0003-100 (P3115)

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
	AA	FOLKMAN, "Tumor angiogenesis: therapeutic implications," New. Eng. J. Med. (1971) 285:1182-1186	
	AB	RISAU, "Mechanisms of angiogenesis," Nature (1997) 386:671-674.	
	AC	KIM, et al., "Inhibition of vascular endothelial growth factor-induced angiogenesis suppresses tumor growth in vivo," Nature (1993) 362:841-844.	
	AD	HANAHAN and FOLKMAN, "Patterns and emerging mechanisms fo the angiogenic switch during tumorigenesis," Cell (1996) 86:353-364.	
	AE	HANAHAN, "Signalling vascular morhogenesis and maintenance," Science (1997) 277:48-50.	
	AF	HANAHAN and WEINBERG, "The hallmarks of cancer," Cell (2000) 100:57-70.	
	AG	FOLKMAN and D'AMORE, "Blood vessel formation: what is its molecular basis?", Cell (1996) 87:1153-1155.	
	AH	YANCOPOULOS, et al., "Vascular-specific growth factors and blood vessel formation," Nature (2000) 407:242-248.	
	AI	INGBER and FOLKMAN, "How does extracellular matrix control capillary morphogenesis?", Cell (1989) 58:803-805.	
	AJ	RAMSAUER and D'AMORE, "Getting tie(2)d up in angiogenesis," J. Clin. Investig. (2002) 110:1615-1617.	
	AK	BETSHOLTZ, et al., "Developmental roles of platelet -derived growth factors," BioEssays (2001) 23:494-507.	

Examiner Signature		Date Considered	

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[1] Applicant's unique citation designation number (optional). [2] Applicant is to place a check mark here if English language Translation is attached.
This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Sheet 2 of 9

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	AL	FONG, et al., "Role of the Flt-1 receptor tyrosine kinase in regulating the assembly of vascular endothelium," Nature (1995) 376:66-70.	
	AM	MAISONPIERRE, et al., "Angiopoietin-2, a natural antagonist for tie2 that disrupts in vivo angiogenesis," Science (1997) 277:55-60.	
	AN	SATO, et al., "tie-1 and tie-2 define another class of putative receptor tyrosine kinase genes expressed in early embryonic vascular system," Proc. Natl. Acad. Sci. USA (1993) 90:9355-9358.	
	AO	SCHNURCH and RISAU, "Expression of the tie-2, a member of a novel family of receptor tyrosine kinases, in the endothelial cell lineage," Development (1993) 119:957-968.	
	AP	DUMONT, et al., "Dominant-negative and targeted null mutations in the endothelial receptor tyrosine kinase, tek, reveal a critical role in vasculogenesis of the embryo," Genes Dev. (1994) 8:1897-1909.	
	AQ	COOGAN, et al., "Expression of tie2/tek in breast tumor vasculature provides a new marker for evaluation of tumor angiogenesis," Br. J. Cancer (1998) 77:51-56.	
	AR	SATO, et al., "Distinct roles of the receptor tyrosine kinases tie-1 and tie-2 in blood vessel formation," Nature (1995) 376:70-74.	
	AS	SURI, et al., "Requisite role of angiopoietin-1, a ligand for the TIE2 receptor during embryonic angiogenesis," Cell (1996) 87:1171-1180.	
	AT	GALE and YANCOPOULOS, "Growth factors acting via endothelial cell-specific receptor tyrosine kinases: VEGFs, angiopoietins, and ephrins in vascular development," Genes Dev. (1999) 13:1055-1066.	
	AU	SURI, et al., "Increased vascularization in mice overexpressing angiopoietin-1," Science (1998) 282:468-471.	
	AV	THURSTON, et al., "Leakage-resistant blood vessels in mice transenically overexpressing angiopoietin-1," Science (1999) 286:2511-2514.	

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Sheet 3 of 9

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	AW	THURSTON, et al., "Angiopoietin-1 protects the adult vasculature against plasma leakage," Nature Med. (2000) 6:460-463.	
	AX	STRATMANN, et al., "Cell type-specific expression of angiopoietin-1 and angiopoietin-2 suggests a role in glioblastoma angiogenesis," Am. J. Pathol. (1998) 153:1459-1466.	
	AY	WITZENBICHLER, et al., "Chemotactic properties of angiopoietin-1 and -2, ligands for the endothelial-specific receptor tyrosine kinase tie2.," J. Biol. Chem. (1998) 273:18514-18521.	
	AZ	CARLSON, et al., "Direct cell adhesion to the angiopoietins mediated by integrins," J. Biol. Chem. (2001) 276:26516-26525.	
	BA	PAPAPETROPOULOS, et al., "Angiopoietin-1 inhibits endothelial cell apoptosis via the Akt/survivin pathway," J. Biol. Chem. (2000) 275:9102-9105.	
	BB	KIM, et al., "Angiopoietin-1 regulates endothelial cell survival through the phosphatidylinositol 3'-kinase/Akt signal transduction pathway," Circulation Res. (2000) 86:24-29.	
	BC	HAYES, et al., "Angiopoietin-1 and its receptor Tie-2 participate in the regulation of capillary-like tubulin formation and survival of endothelial cells," Microvasc. Res. (1999) 58:224-237.	
	BD	OH, et al., "Hypoxia and vascular endothelial growth factor selectively upregulate angiopoietin-2 in bovine microvascular endothelial cells," J. Biol. Chem. (1999) 274:15732-15739.	
	BE	MANDRIOTA and PEPPER, "Regulation of angiopoietin-2 mRNA levels in bovine microvascular endothelial cells by cytokines and hypoxia," Circulation Res. (1998) 83:852-859.	
	BF	KIM, et al., "Tumor necrosis factor-alpha upregulates angiopoietin-2 in human umbilical vein endothelial cells," Biochem. Biophys. Res. Comm. (2000) 269:361-365.	
	BG	KIM, et al., "Angiopoietin-1 induces endothelial cell sprouting through the activation of focal adhesion kinase and plasmin secretion," Circulation Res. (2000) 86:952-959.	

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Sheet 4 of 9

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	BH	VALENZUELA, et al., "Angiopoietins 3 and 4: diverging gene counterparts in mice and humans," Proc. Natl. Acad. Sci. USA (1999) 96:1904-1909.	
	BI	SIEMEISTER, et al., "Two independent mechanisms essential for tumor angiogenesis: inhibition fo human melanoma xenograft growth by interfering with eiter the vascular endothelial growth factor receptor pathway of the tie-2 pathway," Cancer Res. (1999) 59:3185-3193.	
	BJ	MILLAUER, et al., "Glioblastoma growth inhibited in vivo by a dominant-negative Flk-1 mutant," Nature (1994) 367:576-579.	
	BK	GOLDMAN, et al., "Paracrine expression of a native soluble vascular endothelial growth factor receptor inhibits tumor growth, metastsis, and mortality rate," Proc. Natl. Acad. Sci. USA (1998) 95:8795-8800.	
	BL	AHMAD, et al., "The effects of angiopoietin-1 and -2 on tumor growth and angiogenesis in human colon cancer," Cancer Res. (2001) 61:1255-1259.	
	BM	ETOH, et al., "Angiopoietin-2 is related to tumor angiogenesis in gastric carcinoma:possible in vivo regulation via induction of proteases," Cancer Res. (2001) 61:2145-2153.	
	BN	HAWIGHORST, et al., "Activation of the tie2 receptor by angiopoietin-1 enhances tumor vessel maturation nad impairs squamous cell carcinoma growth," Am. J. Pathol. (2002) 100:1381-1392.	
	BO	KOGA, et al., "Expression of angiopoietin-2 in human glioma cells and its role for angiogenesis," Cancer Res. (2001) 61:6248-6254.	
	BP	PAPETTI and HERMAN, "Mechanisms of normal and tumor-derived angiogenesis," Am. J. Physiol. Cell Physiol. (2002) 282:C947-C970.	
	BQ	TEICHERT-KULISZEWSKA, et al., "Biological action of angiopoietin-2 in a fibrin matrix model of angiogenesis is associated with activation if Tie2," Cardiovasc. Res. (2001) 49:659-670.	

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	BS	YU and STAMENKOVIC, "Localization of matrix metalloproteinase 9 to the cell surface provides a mechanism for CD44-mediated tumor invasion," Genes Dev. (1999) 13:35-48.	
	BT	HUNGERFORD and LITTLE, "Developmental biology of the vascular smooth muscle cell: building a multilayed vessel wall," J. Vasc. Res. (1999) 36:2-27.	
	BU	GALE, et al., "Angiopoietin-2 is required for postnatal angiogenesis and lymphatic patterning, and only the latter role is rescued by angiopoietin-1," Devel. Cell (2002) 3:411-423.	
	BV	SHYU, et al., "Direct intramuscular injection of plasmid DNA encoding angiopoietin-1 but not angiopoietin-2 augments revascularization in the rabbit ischemic hindlimb," Circulation (1998) 98:2081-2087.	
	BW	KIM, et al., "Angiopoietin-2 at high concentration can enhance endothelial cell survival through the phosphatidylinositol 3'-kinase/Akt signal transduction pathway," Oncogene (2000) 19:4549-4552.	
	BX	LANDER and SELLECK, "The elusive functions of proteoglycans: in vivo veritas," J. Cell Biol. (2000) 148:227-232.	
	BY	IOZZO, "Matrix metalloproteins: from molecular design to cellular function," Ann. Rev. Biochem. (1998) 67:609-652.	
	BZ	IOZZO and SAN ANTONIO, "Heparan sulfate proteoglycans: heavy hitters in the angiogenesis arena," J. Clin. Investig. (2001) 108:349-355.	
	CA	FIEDLER, et al., "Angiopoietin-1 and angiopoietin-2 share the same binding domains in the tie-2 receptor involving the first Ig-like loop and the epidermal growth factor-like repeats," J. Biol. Chem. (2003) 278:1721-1727.	
	CB	YU, et al., "Induction of apoptosis of metastatic mammary carcinoma cells in vivo by disruption of tumor cell surface CD44 function," J. Exp. Med. (1997) 186:1985-1996.	
	CC	KONTOS, et al., "Tyrosine 1011 of tie2 is the major site of association of p85 and is required for activation of phosphatidylinositol 3-kinase and Akt," Mol. Cell. Biol. (1998) 18:4131-4140.	

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	CD	FIDLER and ELLIS, "The implications of angiogenesis for the biology and therapy of cancer metastasis," Cell (1994) 79:185-188.	
	CE	FIDLER, "Angiogenetic heterogeneity: regulation of neoplastic angiogenesis by the organ microenvironment," J. Natl. Cancer Inst. (2001) 93:1040-1041.	
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	CI	GENGRINOVITCH, et al., "Glypican-1 is a VEGF165 binding proteoglycan that acts as an extracellular chaperone for VEGF165," J. Biol. Chem. (1999) 274:10816-10822.	
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Sheet 7 of 9

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Filing Date	February 27, 2004
First Named Inventor	Qin Yu
Art Unit	Not Yet Assigned
Examiner Name	Not Yet Assigned
Attorney Docket Number	UPN0003-100 (P3115)

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	CO	POLTORAK, et al., "VEGF145, a secreted vascular endothelial growth factor isoform that binds to extracellular matrix," J. Biol. Chem. (1997) 272:7151-7158.	
	CP	ROBINSON and STRINGER, "The splice variants of vascular endothelial growth factor (VEGF) and their receptors," J. Cell Sci. (2001) 114:853-865.	
	CQ	RUHRBERG, "Endogenous inhibitors of angiogenesis," J. Cell Sci. (2001) 114:3215-3216.	
	CR	SAARISTO, et al., "Mechanisms of angiogenesis and their use in the inhibition of tumor growth and metastasis," Oncogene (2000) 19:6122-6129.	
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	CW	VU, et al., "MMP-9/gelatinase-B is a key regulator of growth plate angiogenesis and apoptosis of hypertrophic chondrocytes," Cell (1998) 93:411-422.	
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	CY	BLOEMENDAL, et al., "New strategies in anti-vascular cancer therapy," Eur. J. Clin. Investig. (1999) 29:802-809.	

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	CZ	HARFOUCHE, et al., "Mechanisms which mediate the antiapoptotic effects of angiopoietin-1 on endothelial cells," Microvasc. Res. (2002) 64:135-147.	
	DA	HIRAOKA, et al., "Matrix metalloproteinases regulate neovascularization by acting as pericellular fibrinolysins," Cell (1998) 95:365-377.	
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	DC	FANG, et al., "Matrix metalloproteinase-2 is required for the switch to the angiogenic phenotype in a tumor model," Proc. Natl. Acad. Sci. USA (2000) 97:3884-3889.	
	DD	PFEIFER, et al., "Suppression of angiogenesis by lentiviral delivery of PEX, a noncatalytic fragment of matrix metalloproteinase 2," Proc. Natl. Acad. Sci. USA (2000) 97:12227-12232.	
	DE	STERNLICHT and WERB, "How matrix metalloproteinases regulate cell behavior," Ann. Rev. Cell Dev. Biol. (2001) 17:463-516.	
	DF	SILLETTI, et al., "Disruption of matrix metalloproteinase 2 binding to integrin alphavbeta3 by an organic molecule inhibits angiogenesis and tumor growth in vivo," Proc. Natl. Acad. Sci. USA (2001) 98:119-124.	
	DG	SIPES, et al., "Cooperation between thrombospondin-1 type 1 repeat peptides and alphavbeta3 integrin ligands to promote melanoma cell spreading and focal adhesion kinase phosphorylation," J. Biol. Chem. (1999) 274:22755-22762.	
	DH	VISCONTI, et al., "Orchestration of angiogenesis and arteriovenous contribution by angiopoietins and vascular endothelial groth factor (VEGF)," Proc. Natl. Acad. Sci. USA (2002) 99:8219-8224.	
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	DJ	YU and STMENKOVIC, "Cell surface-localized matrix metalloproteinase-9 protelytically activates TGF-beta and promotes tumor invasion and angiogenesis," Genes Dev. (2000) 14:163-176.	

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	DK	McFALL and RAPRAEGER, "Characterization of the high affinity cell-binding domain in the cell surface proteoglycan syndecan-4," J. Biol. Chem. (1998) 273:28270-28276.	
	DL	OLSON, et al., "High affinity binding of latent matrix metalloproteinase-9 to the alpha2(IV) chain of collagen IV," J. Biol. Chem. (1998) 273:10672-10681.	
	DM	BROOKS, et al., "Localization of matrix metalloproteinase MMP-2 to the surface of invasive sells by interaction with integrin alphavbeta3," Cell (1996) 85:683-693.	
	DN	MOYON, et al., "Selective expression of angiopoietin 1and 2 in mesenchymal cells surrounding veins and arteries of the avian embryo," Mechs. Devel. (2001) 106:133-136.	
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	DR	JOUSSEN, et al., "Suppression of diabetic retinopathy with angiopoietin-1," Am. J. Pathol. (2002) 160:1683-1693.	
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